

TRANSLATION

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>P05078300</b>	<b>FOR FURTHER ACTION</b>	See Form PCT/IPEA/416
International application No. <b>PCT/JP2004/018235</b>	International filing date ( <i>day/month/year</i> ) <b>01.12.2004</b>	Priority date ( <i>day/month/year</i> ) <b>01.12.2003</b>
International Patent Classification (IPC) or national classification and IPC <b>C07K5/083, A61K38/00, A61P9/12, A61P43/00</b>		
Applicant <b>MEIJI DAIRIES CORPORATION</b>		

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>8</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> (<i>sent to the applicant and to the International Bureau</i>) a total of <u>1</u> sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (<i>sent to the International Bureau only</i>) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>																										
<p>4. This report contains indications relating to the following items:</p> <table><tr><td><input checked="" type="checkbox"/></td><td>Box No. I</td><td>Basis of the report</td></tr><tr><td><input type="checkbox"/></td><td>Box No. II</td><td>Priority</td></tr><tr><td><input type="checkbox"/></td><td>Box No. III</td><td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td></tr><tr><td><input type="checkbox"/></td><td>Box No. IV</td><td>Lack of unity of invention</td></tr><tr><td><input checked="" type="checkbox"/></td><td>Box No. V</td><td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VI</td><td>Certain documents cited</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VII</td><td>Certain defects in the international application</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VIII</td><td>Certain observations on the international application</td></tr></table>			<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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Date of submission of the demand		Date of completion of this report																								
Name and mailing address of the IPEA/JP		Authorized officer																								
Facsimile No.		Telephone No.																								

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. I

Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of:
- ☐ international search (Rule 12.3 and 23.1(b))
- ☐ publication of the international application (Rule 12.4)
- ☐ international preliminary examination (Rule 55.2 and/or 55.3)
2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):
- ☐ the international application as originally filed/furnished
- ☒ the description:
- pages 1-8 \_\_\_\_\_ as originally filed/furnished
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☒ the claims:
- nos. \_\_\_\_\_ as originally filed/furnished
- nos.\* \_\_\_\_\_ as amended (together with any statement) under Article 19
- nos.\* 1-12 \_\_\_\_\_ received by this Authority on 29.09.2005
- nos.\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☒ the drawings:
- sheets fig. 1 \_\_\_\_\_ as originally filed/furnished
- sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1. Statement			
Novelty (N)	Claims	1-7, 9-12	YES
	Claims	8	NO
Inventive step (IS)	Claims	1	YES
	Claims	2-12	NO
Industrial applicability (IA)	Claims	1-12	YES
	Claims		NO
2. Citations and explanations (Rule 70.7)			
	Document 1: JP 2003-511063 A (Saint Louis University), 25 March 2003, claims		
	Document 2: JP 6-279491 A (The Nippon Synthetic Chemical Industry Co., Ltd.), 04 October 1994, entire text		
	Document 3: JP 6-277090 A (The Nippon Synthetic Chemical Industry Co., Ltd.), 04 October 1994, entire text		
	Document 4: JP 6-277091 A (The Nippon Synthetic Chemical Industry Co., Ltd.), 04 October 1994, entire text		
	Document 5: JP 7-101982 A (The Nippon Synthetic Chemical Industry Co., Ltd.), 18 April 1995, entire text		
	Document 6: JP 2002-121199 A (Kabushiki Kaisha Shimaya), 23 April 2002, entire text		
	Claim 8		
	The invention set forth in claim 8 lacks novelty and does not involve an inventive step in the light of documents 2 to 5 cited in the international search report.		
	Documents 2 to 5 disclose protease hydrolysates of		

Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

casein.

The invention set forth in claim 8 pertains to peptides with an action that inhibits the angiotensin converting enzyme, which have an amino acid sequence represented by one of SEQ ID NO: 1 to 3 with one or more amino acids added thereto; therein, claim 8 does not delimit an upper limit for the length of the amino acid sequences that are added thereto.

The tripeptides set forth in the present application are obtained by hydrolysing casein, and thus it is likely that the casein or the casein hydrolysates from the inventions disclosed in documents 2 to 5 also include a peptide with an action that inhibits the angiotensin converting enzyme, which has an amino acid sequence represented by one of SEQ ID NO: 1 to 3 with one or more amino acids added thereto.

Such being the case, the invention set forth in claim 8 cannot be differentiated from the inventions disclosed in documents 2 to 5.

Claims 2 to 7 and 9 to 12

The inventions set forth in claims 2 to 7 and 9 to 12 do not involve an inventive step in the light of documents 2 to 6 cited in the international search report.

The inventions set forth in claims 4 to 6 pertain to peptides with an action that inhibits the angiotensin converting enzyme, which have an amino acid sequence represented by one of SEQ ID NO: 1 to 3 with one or more amino acids added thereto; therein, claims 2 to 7 and 9 to 12 do not delimit an upper limit for the length of the amino acid sequences that are added thereto, and thus the

Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

scope of the peptides in question includes the peptides that are produced when casein is partially hydrolysed by a protease.

Documents 2 to 5 indicate that tripeptides with an action that inhibits the angiotensin converting enzyme were obtained by subjecting casein, which is a milk protein, to hydrolysis by means of a protease. In addition, documents 2 to 5 also indicate that the obtained peptides can be used as medicaments against disorders that are associated with abnormalities of the angiotensin converting enzyme.

Meanwhile, document 6 indicates that tripeptides with an action that inhibits the angiotensin converting enzyme were obtained by using a protease such as *Aspergillus oryzae* in order to hydrolyze fish meat such as dried bonito meat.

Documents 2 to 6 all present methods for obtaining tripeptides with an action that inhibits the angiotensin converting enzyme by subjecting animal proteins to hydrolysis by means of a protease; therefore, it would have been easy for a person skilled in the art to conceive of obtaining novel peptides with an action that inhibits the angiotensin converting enzyme by using the protease disclosed in document 6 in the inventions disclosed in documents 2 to 5.

In the written response, the applicant asserts that the inventions disclosed in documents 2 to 5 do not employ *Aspergillus oryzae*, and thus are different from the inventions set forth in the present application; asserts that it is impossible to obtain the tripeptides that are set forth in the present application by simply treating casein with *Aspergillus oryzae*; and asserts that

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Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

the Met-Ala-Pro tripeptide set forth in the present application exhibits a prominent effect in comparison to the tripeptides that are disclosed in the abovementioned documents.

However, the scope of the inventions set forth in claims 4 to 6 includes the peptides that are produced when casein is partially hydrolysed by a protease, as is indicated above. In addition, it is considered to be easy for a person skilled in the art to conceive of separating tripeptides from the other hydrolysates of a protein such as casein by means of the techniques that are disclosed in documents 2 to 5.

With regards to the effects of the inventions in question, there are no specific assertions with regards to the tripeptides represented by SEQ ID NO: 2 to 3, and thus the peptides in question cannot be considered to exhibit an especially prominent effect that would have been impossible to predict.

Such being the case, the inventions set forth in claims 2 to 7 and 9 to 12 do not involve an inventive step.

#### Claim 1

The invention set forth in claim 1 involves an inventive step in relation to the documents that are cited in the international search report. The peptide with an action that inhibits the angiotensin converting enzyme, which has an amino acid sequence represented by SEQ ID NO: 1, is not disclosed in any of the documents that are cited in the international search report; furthermore, the invention in question exhibits a prominent effect in comparison to the tripeptides

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<div>disclosed in the documents that are cited in the international search report.</div>	

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:
  - a. type of material
    - ☒ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material
    - ☐ in written format
    - ☒ in computer readable form
  - c. time of filing/furnishing
    - ☒ contained in the international application as filed
    - ☐ filed together with the international application in computer readable form
    - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
    - ☐ received by this Authority as an amendment\* on \_\_\_\_\_
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

\* If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."